RATIONALE DOCUMENT FOR THE INTERIM MAXIMUM ACCEPTABLE CONCENTRATION FOR N-NITROSODIMETHYLAMINE (NDMA) IN DRINKING WATER

APRIL 1991

Ontario
Environment
Environnement

ISBN 0-7729-8434-4

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APRIL 1991

Cette publication technique
n'est disponible qu'en anglais

log 16-3505-1991
PIBS 1544

FOREWORD

This document was prepared to summarize the relevant information considered by Environment Ontario in selecting an Interim Maximum Acceptable Concentration (IMAC) for N-nitrosodimethylamine (NDMA) in Ontario drinking water. Hazardous Contaminants Coordination Branch prepared the report in consultation with West Central Region, Water Resources Branch, Laboratory Services Branch and Air Resources Branch.

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1.0 BACKGROUND

N-Nitrosodimethylamine (NDMA) is a simple organic compound that exists as a stable liquid under ambient temperatures and conditions. It is a potent, non-threshold carcinogen in a wide variety of animal species, both mammalian and non-mammalian. The U.S. Environmental Protection Agency (EPA) and the International Agency for Research on Cancer (IARC) have classified NDMA as a probable human carcinogen.

NDMA is no longer used commercially, but it may be an inadvertent by-product of some industries employing amines or nitrites under acidic conditions. It may therefore occur in the discharges from rubber manufacturing, leather tanning, pesticide manufacturing, food processing plants or sewage treatment plants.

In November, 1989, high levels of NDMA were detected by the Ministry of the Environment in the drinking water of Elmira, Ontario. An Interim Maximum Acceptable Concentration (IMAC) of 14 ppt (parts per trillion) in drinking water was adopted from a U.S. EPA risk assessment (REF 1) to control NDMA discharges from a local rubber chemicals plant.

Given the importance of the need for a current and scientifically defensible guideline for drinking water the Ministry established in May, 1990, an Interministry Expert Committee, with representatives from the Ministries of Environment, Health and Labour and from the Regional Municipality of Waterloo. This committee was to recommend the scientific basis for NDMA guidelines in air, water and soil.

In its scientific criteria document (REF 2), the Interministry Expert Committee adopted a risk assessment framework to evaluate the available scientific data on NDMA. Risk assessment consists of four phases: hazard identification, exposure assessment, dose response assessment and risk characterization. Exposure was assessed from a multimedia perspective since NDMA is found in several environmental compartments and human exposure can occur through multiple exposure pathways. This rationale document describes the Expert Committee's findings and recommendations.

In developing an IMAC for drinking water the Ministry considered the Expert Committee's recommendations on the risks to health of NDMA and relevant risk management factors such as analytical detection limits and relative risks from other sources of exposure.

2.0 HAZARD IDENTIFICATION

The hazard identification phase for NDMA required identification of its potentially adverse environmental and health impacts, including the most sensitive toxic endpoint.

NDMA is of low to moderate toxicity to aquatic and terrestrial animals when exposure is short term. However, genotoxic studies have demonstrated it to be strongly mutagenic in most test systems. Long term exposure studies have shown it to be both toxic and carcinogenic in a wide variety of animal species, with the target organ being the liver. Although human

epidemiological exposure data are not available, the U.S. EPA and the IARC have classified NDMA as a probable human carcinogen.

The scientific criteria document has identified carcinogenicity as the most sensitive endpoint for NDMA, with human health as the critical endpoint in evaluating risk of exposure.

3.0 EXPOSURE ASSESSMENT

Environmental assessment identifies the major pathways of exposure to NDMA, the levels of exposure from each pathway and the total exposure of humans from all pathways.

3.1 Air

NDMA has a low vapour pressure and is rarely detected in ambient air. NDMA released to the atmosphere is not likely to adsorb to airborne particulate matter and is expected to exist almost entirely in the vapour phase. In daylight, it degrades rapidly by direct photolysis. Reaction with hydroxyl radicals or ozone molecules is expected to be too slow to be environmentally significant.

NDMA has been measured at urban sites and at or near industrial sites in the U.S.A. In Ontario, very low levels (ng/m^3) have been detected near industrial locations in Elmira. In a limited survey of five Ontario cities, NDMA was non-detectable at the current detection limit of 2 ng/m^3. Assuming that ambient air contains less than the current analytical detection limit of 2 ng/m^3 NDMA, and that the average inhalation rate of a 70 kg individual is 20 m^3/day, the daily intake is estimated to be less than 40 ng.

3.2 Water

NDMA is highly water soluble and has a low octanol/water partition coefficient. This means that NDMA is not likely to bioaccumulate, adsorb to particulates or to volatilize to any significant extent. This further signifies that NDMA has the potential to leach into and migrate within groundwater supplies. NDMA has been demonstrated to degrade rapidly through photolysis in shallow surface waters. However, in groundwater and in the absence of light, NDMA has the potential to persist. Thus, exposure through contaminated drinking water could be significant.

Exceedances of the 14 ppt IMAC have occurred in drinking water supplies within the Grand River System, but levels since February, 1990, have been below 10 ppt. The Drinking Water Surveillance Program of the Ministry had previously found no detectable levels of NDMA at over 40 sites elsewhere in Ontario using a detection limit of 50 ppt or greater. Assuming that water levels are below the detection limits reported in the range of 2-10 ppt and that daily consumption is 1.5 L/day, the daily intake is estimated to be less than 3 to 15 ng.

3.3 Soil

On soil surfaces, NDMA would be rapidly removed by photolysis and volatilization. Once incorporated into subsurface soil, however, it will be highly mobile, with the potential to migrate into groundwater supplies. No data, however, are available for Ontario or U.S. soil to allow an estimation of exposure through this route.

3.4 Food

Diet is an important pathway for NDMA exposure. NDMA has been measured in several processed foods: nitrate or nitrite-cured meat products (<2 -17 ug/kg); malt-based beverages or other foods dried directly by hot flue gases (<0.05 - 0.7 ug/kg); fish and seafood (<0.1 - 4.2 ug/kg); and other categories, including cheese (<1 - 68 ug/kg). Surveys of Canadian food samples have been carried out by the Health Protection Branch, Health and Welfare Canada.

Dietary inputs are difficult to estimate, because humans may consume both NDMA precursors and inhibitors through a variety of foods. However, using the data from the Health and Welfare surveys, a **minimum** estimate of the average daily intake is 200 ng/day.

4.0 DOSE RESPONSE ASSESSMENT

Dose response relationships define the relationship between the magnitude of exposure and the probability of environmental or health effects. The toxic endpoint of NDMA is its carcinogenicity. Dose response assessment thus requires the selection of a suitable tumour incidence data set and an appropriate mathematical extrapolation model to define the relationship between the dose of NDMA and tumour incidence.

4.1 Selection of Tumour Incidence Data

Epidemiological data for human exposure to NDMA are not available. Hence, reliance must be placed on suitable animal studies. Four bioassay data sets were identified that met the EPA criteria for technical adequacy of animal carcinogenicity studies. Of these, the most appropriate is a major research program on nitrosamine carcinogenesis commissioned in 1978 by the British Ministry of Agriculture, Fisheries and Food, referred to in the scientific criteria document as the British Industrial Biological Research Association (BIBRA) study. The study involved a large number of animals exposed to a wide range of NDMA concentrations in drinking water. Total liver tumours, both benign and malignant, were used in the tumour incidence data set.

4.2 Selection of Mathematical Extrapolation Model

Risks at low exposure levels normally encountered in the environment cannot be measured directly. A number of different mathematical models have been used by various organizations to derive health-based numbers for NDMA. The models have been developed to extrapolate

from high doses inducing cancer in animal studies to predict risk at low level exposures in humans. The models are subject to considerable uncertainty and different models may yield very different estimates of risk using the same set of biological data.

Three major models were applied to the BIBRA data set: the Linear Multistage model; the Model Free Approach; and the Weibull model.

The Linear Multistage model is a polynomial model which uses arbitrary constants to fit monotonically increasing sets of dose response data. It was rejected because it is the least conservative of the three models and does not consider time to tumour development.

The Model-Free Approach does not use parameters. It is the most conservative of the three models, with a tendency to calculate slope estimates 30% to 100% higher than the Linear Multistage Model. It was rejected because it employs only a single point of the large BIBRA data set for NDMA. Furthermore, it has not yet been peer reviewed or published.

The Weibull Model was selected as most appropriate by the Interministry Expert Committee, because it takes into account the time to tumour development, an important consideration for the BIBRA study. It is also the model used by the EPA, the California Department of Public Health Services, and the Regional Municipality of Waterloo.

The Weibull model is statistical and represents the relationship between lifetime exposure to NDMA and tumour incidence. Cancer potency is estimated from the slope of the dose response curve. Results are moderately conservative, with a slope factor for humans of 51/mg/kg/day.

5.0 RISK CHARACTERIZATION

Risk characterization is the integration of exposure assessment and dose response assessment to delineate the nature and magnitude of the risk of estimated exposure. The magnitude and type of risk from each route of exposure is assessed and evaluation made of its contribution to total risk. In view of the uncertainties inherent in predictions of risk, assumptions tended to be conservative so that risk estimates would be protective of human health.

Total human exposure to NDMA in air, water, diet and soil should be kept in the range of negligible lifetime cancer risk. A range of 10^{-5} to 10^{-6} has generally been used for this purpose by other jurisdictions The slope factor of 51/mg/kg/day, calculated from the Weibull model, was used to estimate the incremental lifetime cancer risks associated with unit doses of exposure to NDMA. Using the estimates of exposure obtained in the exposure assessment phase, the following health-based numbers and associated incremental lifetime cancer risks were derived.

5.1 Drinking Water

For drinking water, it was assumed that a 70 kg individual consumes 1.5 L/day. The health-based numbers are presented in Table 1.

Table 1. Levels of NDMA in Drinking Water and Associated Incremental Lifetime Cancer Risks

Level of NDMA in Water	Incremental Lifetime Cancer Risk
9 ppt	10^{-5}
0.9 ppt	10^{-6}

5.2 Air

For ambient air, it was assumed that a 70 kg individual inhales 20 m^3 a day and exposure is averaged over one year. In developing an air guideline, the Ministry of the Environment sets levels for 24 hour and one-half hour averaging times, which correspond to five and fifteen times the annual average value, respectively. The health-based numbers for ambient air are presented in Table 2.

Table 2. Levels of NDMA in Ambient Air and Associated Incremental Lifetime Cancer Risks

Level of NDMA in Air	Incremental Lifetime Cancer Risk
0.7 ng/m^3	10^{-5}
0.07 ng/m^3	10^{-6}

5.3 Soil

Due to lack of data, no recommendations for soil can be made at this time.

5.4 Food

With regard to food, the average daily intake of NDMA is estimated to be approximately 200 ng/day, a level which corresponds to an incremental lifetime risk of 2×10^{-4}.

6.0 RISK MANAGEMENT CONSIDERATIONS

The critical need, for the Ministry at this time is the development of a limit for NDMA in drinking water. An Interim Maximum Acceptable Concentration (IMAC) is the term used to describe limits for substances of current concern with known chronic effects in mammals and for which there are no established maximum acceptable concentrations. Although toxicological, epidemiological and health data are available for such substances the data are subject to public and scientific debate before agreement on a maximum acceptable concentration. The IMAC will generally be a conservative value subject to change as more precise information becomes available. When a substance is detected at a concentration above its IMAC, it will signal the need for more sampling and investigation. Requirements for corrective action will be on a case-by-case basis. (REF 3)

In general, for a non-threshold probable human carcinogen, such as NDMA, health-based guidelines should be set at a level of risk that is considered negligible - typically set at the 10^{-5} to 10^{-6} unless risk management considerations do not permit (REF 4). The relevant considerations are: ambient concentrations and human exposure levels, analytical detection capability, treatability and effluent control technology, and cost of control. A preliminary assessment of these considerations was undertaken to ascertain if an IMAC set at a negligible risk level would be implementable.

6.1 Background Levels and Human Exposure Levels

Very limited information is available on levels of NDMA in ambient air, surface water, drinking water and effluents. Since the completion of the Expert Committee's Report the Ministry has initiated an NDMA sampling program of representative water supplies across the province. Preliminary results indicate that levels of NDMA are below the detection limit, which for this program ranged from 5 ppt to 10 ppt due to variability in the sampling conditions. For humans, food is the major source of exposure and the average daily intake of NDMA contributes an additional 2×10^{-4} to an individual's lifetime cancer risk. In view of the current exposure from food, it would be prudent to minimize exposure from other sources. As such, water guidelines should be based on a negligible lifetime cancer risk, if possible.

6.2 Analytical Detection Capability

For surveillance and control purposes, the IMAC should be measurable. The analytical methodology developed by the Ministry of the Environment has a detection limit for drinking water of 5 ppt, achievable on a routine basis. The detection limit for wastewater effluents is 10 ppt. This detection limit would allow the IMAC to be set within the negligible lifetime cancer risk range.

6.3 Treatment/Effluent Control Technology and Cost of Control

Limited information is available on effluent control technologies for the treatment and removal of NDMA from the aqueous phase. Photo-oxidation water remediation technology has been applied at the pilot scale level to water contaminated with NDMA. This technology uses

ultraviolet light and studies found that concentrations of NDMA were reduced from levels up to 20 ppb (parts per billion) to below the detection limit of 3 ppt (REF 5). Full-scale implementation of the technology is underway in the community of Elmira by the regional Municipality of Waterloo for the treatment of NDMA contaminated groundwater. The system is designed to treat 500 gallons per minute of contaminated groundwater and reduce levels of NDMA from greater than 20 ppb to below 9 ppt. The capital cost of the treatment component of the system is in the order of $400,000 (REF 6). The technology is also being proposed for use by an industrial facility in the province in the further development of their treatment system for controlling discharges to the environment.

The limited information available at this time precludes an assessment of the need and associated costs for controlling discharges of NDMA across the province.

7.0 REVISED INTERIM MAXIMUM ACCEPTABLE CONCENTRATION FOR NDMA

It is recommended that the IMAC for drinking water be lowered from the current level of 14 ppt to 9 ppt. The revised IMAC can be measured on a routine basis using recently developed analytical methods and represents a risk of 10^{-5}, which is within the range of negligible incremental lifetime cancer risk.

The revised IMAC will be used to assess both drinking water and point source discharges, and where necessary, to control NDMA discharges from sewage treatment plants and direct industrial dischargers.

REFERENCES

1. United States Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office. 1980. Ambient water quality criteria for nitrosamines. Office of Water Regulations and Standards, U.S. Environmental Protection Agency, Washington. D.C. PB81-117756.

2. Ontario Ministry of the Environment, Hazardous Contaminants Co-ordination Branch. 1990. N-Nitrosodimethylamine. Scientific criteria document for multimedia standard development, No. 01-90.

3. Ontario Ministry of the Environment. 1983. Ontario drinking water objectives. Ontario Ministry of the Environment, Toronto.

4. Health and Welfare Canada. 1989. Derivation of maximum acceptable concentrations and aesthetic objectives for chemicals in drinking water. In, Guidelines for Canadian drinking water quality, supporting documentation. Supply and Services, Ottawa.

5. Solarchem Environmental Systems. 1990. Rayox: a second generation enhanced oxidation process for groundwater remediation. Unpublished.

6. Shannon, E. 1991. Personal communication, CH2M HILL Ltd, January 31.